IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Confirmation No.:	6491	Examiner:	A.M. Harris
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Inventor:	Christine A. WHITE *et al.*		

For: Treatment of Chronic Lymphocytic Leukemia using Anti-CD20 Antibodies (as amended)

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APPLICANT'S SUMMARY OF INTERVIEW

Sir:

This paper provides the applicants' summary of the personal interview held on 28 January 2009. This paper is filed within the time stated on the Office's interview summary.

At the interview, Applicants' representatives and Dr. Schenkein discussed issues raised by the last Office action.

First, Dr. Schenkein explained the important distinctions that exist between different B-cell malignancies in which the malignant cells express CD20. He explained that notwithstanding the common factor of CD20 expression, physicians view such diseases as being significantly different disorders requiring different therapeutic approaches. He discussed the different characteristics of various B-cell malignancies and explained why practitioners would have doubted that strategies that were effective for NHL would be effective for other B-cell malignancies generally.

Second, Dr. Schenkein explained that although rituximab had been approved for use in treating NHL patients in 1997, this did not provide him with a reasonable basis at that time for believing that rituximab could be used to treat CLL patients. For example, he explained that he believed the significantly different characteristics of CLL as compared to NHL (e.g., high circulating tumor load vs. localized mass in the lymph node) led him to doubt that rituximab could be used to successfully treat CLL. He also explained that, consistent with his beliefs at the time, he did not attempt to use rituximab to treat his CLL

patients, even when their treatment options were limited. He also explained why his personal experiences would have been shared by other physicians at that time.

Third, Dr. Schenkein explained the distinctions between using radiolabeled vs. unlabeled antibodies. He pointed out that the mechanisms by which a "naked" antibody causes cell death and the mechanism by which a radiolabeled antibody, such as the one described in the Kaminski patent, effects cell killing, differ significantly. In particular, he explained that in radioimmunotherapy (RIT), the antibody is only a passive vehicle for delivering a toxic radioisotope, with no contribution from either cell signaling- or T cell recruitment-based mechanisms, which decreases the significance of the levels of CD20 expression on the B-cell. He explained that this would have directly affected the expectations of a physician considering use of each type of agent to treat CLL.

The examiner asked about the mechanisms of rituximab action in NHL and CLL. Dr. Schenkein explained that the mechanisms by which anti-CD20 antibodies deplete B cells are not understood perfectly, even now. He explained that antibody-initiated cellular signaling, leading to apoptosis, and antibody-dependent cellular cytotoxicity (ADCC), a mechanism that depends on T cell recruitment, are both involved in rituximab treatment of NHL. He explained that both the high density of CD20 expression and the presence of a localized mass of B-cells in the lymph nodes were believed to be important factors in the effectiveness of NHL treatment with rituximab. He explained that, in contrast, B-cells in CLL have much lower levels of CD20 expression and these B-cells are not localized but are disseminated in the bloodstream.

No agreement was reached at the interview in respect of the claims.

Applicant believes that this paper requires no fee but requests that the Director debit any fee needed for entry or consideration of this paper to our Deposit Account No. 18-1260.

Respectfully submitted,

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